

REMARKS

In response to the non-final Office Action mailed February 21, 2007, reconsideration is respectfully requested in view of the above amendments and following remarks. Applicants have amended claim 61 to specify that the claimed polypeptide comprises either SEQ ID NO: 113 or a fragment of SEQ ID NO: 113 which comprises residues 367-375. The above amendments are not to be construed as acquiescence to the Examiner's stated grounds for rejections and are made without prejudice to prosecution of any subject matter removed and/or modified by this amendment in a related divisional, continuation or continuation-in-part application. Following the amendments, claims 19, 61 and 63 are under examination in the application.

Rejection Under 35 U.S.C. § 103

Claims 61, 19 and 63 remain rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Momin *et al.* (U.S. Patent No. 6,146,632), Billing-Mendel *et al.* (U.S. Patent No. 6,130,043), and Apostolopoulos *et al.* (Vaccine, 14(9):930-938, 1996).

The Examiner maintains the position that one of skill in the art would have been motivated to modify the immunogenic composition of Momin *et al.* with the polypeptide of Billing-Mendel *et al.* and administer the immunogenic composition to prostate cancer patients for inducing a Th1-type immune response. The Examiner acknowledges that Billing-Mendel *et al.* does not teach the described polypeptide is a T-cell immunogen, but appears to be of the opinion that this deficiency is not important and not relied upon in the outstanding rejection. The Examiner asserts that the basis on which the rejection was set forth is that one skilled in the art would have been motivated to modify the immunogenic composition of Momin *et al.* with the polypeptide of Billing-Mendel *et al.* and administer the immunogenic composition to prostate cancer patients.

Applicants traverse this rejection.

Momin *et al.* teaches adjuvant compositions comprising MPL and QS21, and their use for preferential stimulation of IgG2a production and a Th1 cell response. Momin *et al.* also teaches generally that the adjuvant compositions can be used in conjunction with tumor antigens where it is desired to stimulate a Th1 immune response.

Billing-Mendel *et al.* teaches a polypeptide of 242 amino acids (SEQ ID NO. 36) expressed in prostate cancer tissue, which shares identity with a portion of the instantly claimed SEQ ID NO. 113. Billing-Mendel *et al.* describes that the polypeptide is a prostate cancer diagnostic marker, and that the polypeptide is used to generate antibodies.

Apostolopoulos *et al.* teaches that induction of a Muc-1 specific humoral immune response (Th2 response) gave poor tumor protection accompanied by little cellular immunity; however, when a Muc-1 specific cellular immune response (Th1 response) was induced, this resulted in significant tumor protection, cytotoxic T lymphocytes, and little antibody production.

Applicants submit that successfully arriving at the presently claimed invention would require a teaching on the part of the prior art that a polypeptide of SEQ ID NO: 113 is, in fact, a human T-cell immunogen and that, in addition, a T-cell epitope is present at residues corresponding to 367-375 of SEQ ID NO: 113. The prior art is deficient on both counts and, accordingly, fails to render the presently claimed invention obvious to one of ordinary skill in the art.

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). Further, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

To the extent that Billing-Mendel has any concern with immune responses, it is with humoral immune responses for generating diagnostic antibodies, not with cellular immune responses for stimulating T-cells. Absent this teaching by Billing Mendel *et al.*, the skilled reviewer of Momin *et al.* would not find motivation to use a polypeptide of Billing-Mendel *et al.* in the adjuvant compositions described by Momin *et al.*, but instead would seek T-cell antigens in order that the cellular immune response to the antigens might be improved using the adjuvant compositions of Momin *et al.* Accordingly, any reasonable expectation of arriving at Applicants' claimed invention, and thereby stimulating a human T-cell response specific for

SEQ ID NO: 113, is clearly founded in Applicants' own disclosure but not in the prior art, which is improper.

Further, Applicants respectfully disagree that the lack of disclosure by Billing-Mendel *et al.* of the T-cell immunogenicity of their described polypeptide is inconsequential to the propriety of this rejection under 35 U.S.C. § 103(a). As noted above, absent this feature being taught by the prior art, one skilled in the art would simply not be motivated to combine polypeptide of Billing-Mendel *et al.* with an immunostimulant that induces a predominantly Th1-type immune response. However, even to the extent that one skilled in the art was, for the sake of discussion, to derive motivation to combine the cited references in the manner suggested by the Examiner, there would have nevertheless been no reasonable expectation of success of successfully eliciting a human T-cell response using the polypeptide, since the prior art is completely silent on this point. In this respect, the Examiner's position is predicated on an impermissible obvious to try standard.

Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Billing-Mendel *et al.* is concerned with humoral B-cell immune responses and describes the production of antibodies. Neither Billing-Mendel *et al.*, Momin *et al.* and/or Apostolopoulos *et al.* teach or suggest that any polypeptide bearing a structural relationship to Applicants' claimed SEQ ID NO: 113 is a T-cell antigen or demonstrate the importance of residues 367-375 of SEQ ID NO: 113 as a naturally processed T-cell epitope. As such, even if the skilled artisan decided to try to combine a polypeptide of Billing-Mendel *et al.* with a Th1-type immunostimulant of Momin *et al.*, there would still be no reasonable expectation that a human T-cell response could even be successfully elicited.

Reconsideration and withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 19, 61 and 63 stand newly rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. According to the Examiner, the claims encompass a genus of polypeptides defined only by 9 amino acids of SEQ ID NO: 113, where the polypeptides may have very different structures and functions from the polypeptide of SEQ ID NO: 113.

Applicants traverse this rejection. For clarity and to advance prosecution, claim 61 has been amended such that the claimed polypeptide is a polypeptide comprising SEQ ID NO: 113 or is a fragment of SEQ ID NO: 113 that contains residues 367-375. The claims are thus drawn with particularity to polypeptides of SEQ ID NO: 113 which minimally contain Applicants' identified T-cell epitope. The claims are not drawn to polypeptides having unknown and/or different structures and functions from the polypeptide of SEQ ID NO: 113. Rather, the claimed polypeptides are defined by both structure (SEQ ID NO: 113 and residues 367-375) and function (effective for stimulating a cytotoxic T lymphocyte response specific for SEQ ID NO: 113).

In light of the present disclosure identifying residues 367-375 of SEQ ID NO: 113 as a naturally processed human T-cell epitope, the skilled artisan would understand and appreciate that Applicants were in clear possession of what is being claimed. It is well known and established in the immunological arts that polypeptide antigens are processed by antigen presenting cells (APC) into smaller peptides, and peptide epitopes are presented on the surface of the APC in association with class I MHC proteins in a manner that allows them to interact with and stimulate T-cells. As described in the specification, residues 367-375 of SEQ ID NO: 113 represent a naturally processed T-cell epitope contained within the P501S polypeptide of SEQ ID NO: 113. Accordingly, the skilled artisan would recognize this region as having high value in the context of developing effective immunotherapeutics and, further, would expect that P501S polypeptides of varying lengths will be processed by APC such that the naturally processed epitope sequence of residues 367-375 of SEQ ID NO: 113 is presented to T-cells. What is important in this respect is that the P501S polypeptide contains this naturally processed epitope sequence, less so the extent of additional P501S sequence flanking the epitope. Thus, it would

be recognized that P501S polypeptides of varying lengths, as claimed, may be used in the context of the invention while still achieving a T-cell immune response against this naturally processed epitope. Reconsideration of this rejection is requested.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,
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